

IN THE SPECIFICATION

[0070] Cyclosporins are a group of nonpolar cyclic oligopeptides (some of which have immunosuppressant activity) produced by the genus ~~Topyeladium~~ Tolypocladium, including, e.g. ~~Topyeladium~~ Tolypocladium inflatum Gams (formerly designated as Trichoderma polysporum), ~~Topyeladium~~ Tolypocladium terricola and other fungi imperfecti. The major component, cyclosporin A (cyclosporin or CsA), has been identified along with several other lesser metabolites, for example, cyclosporins B through Z, some of which exhibit substantially less immunosuppressive activity than cyclosporin A. A number of synthetic and semi-synthetic analogs have also been prepared. See generally Jegorov et al., Phytochemistry, 38: 403-407 (1995). The present invention comprehends natural, semi-synthetic and synthetic analogs of cyclosporins.

[0081] Cyclosporins, including cyclosporins A through Z but particularly cyclosporin A (cyclosporin), cyclosporin F, cyclosporin D, dihydro cyclosporin A, dihydro cyclosporin C, acetyl cyclosporin A, PSC-833, SDZ-NIM 811² (both from Sandoz Pharmaceutical Corp.), and related oligopeptides produced by species in the genus ~~Topyeladium~~ Tolypocladium. The structures of cyclosporins A-Z are described in Table 1 below.

²SDZ-NIM 811 is (Me-Ile-4)-cyclosporin, an antiviral, non-immunosuppressive cyclosporin.